

REMARKS

Claims 1-28 are presently pending in this application. Claims 1-3, 5, 8, 14-17, 21 and 27 stand rejected under 35 U.S.C. §102(b). Claims 4, 6, 7, 9-13, 18-20, 22-26 and 28 are objected to for being dependent on a rejected claim. Claims 29-53 are withdrawn from consideration. Reconsideration of this application in light of the following remarks is respectfully requested.

Rejection under 35 U.S.C. 102(b)

Claims 1-3, 5, 8, 14-17, 21 and 27 stand rejected under 35 U.S.C. §102(b) as allegedly anticipated by Schantz et al., *J. AOAC* 61:96-99 (1978) ("Schantz") in the Office Action mailed on February 26, 2004. This rejection maintained for the reasoning first put forth in the Office Action mailed on June 5, 2002. This rejection is respectfully traversed.

The Office Action mailed on June 5, 2002 (paper number 15) states that Schantz teaches a solvent composition comprising purified botulinum type A toxin in acetate buffer having a pH of 4.2 for at least two years at room temperature, preferably 18-24°C. The Office Action indicates that pH 4.2 is "about 5" and that "room temperature falls between the claimed range of 10-30°C or even between 0-10°C based on location, is inherent from the teaching of the prior art."

The Office Action mailed on February 26, 2003 (paper number 19), further states that the "...specification does not contain a precise description of what pH must be included or excluded from the recitation of 'about' pH 5.0. Therefore Schantz's pH of 4.2 is viewed as being encompassed in the scope of the limitation in the instant claims: i.e., the lower range of 'about pH 5.0.'" As noted above, the maintenance of this rejection is respectfully traversed.

Claim 1 is directed to a stable liquid pharmaceutical botulinum toxin formulation comprising a pharmaceutically acceptable buffer capable of providing a buffered pH range between about pH 5 and pH 6, and purified botulinum toxin, wherein the formulation is stable as a liquid for at least one year at a temperature between about 0°C and 10°C.

Claim 16 is directed to a stable liquid pharmaceutical botulinum toxin formulation comprising a pharmaceutically acceptable buffer capable of providing a buffered pH range between about pH 5 and pH 6, and purified botulinum toxin, wherein the formulation is stable as a liquid for at least one year at a temperature between about 10°C and 30°C.

Argument regarding pH 4.2

Applicants' arguments presented in the Reply filed December 5, 2002, are maintained here. As noted therein, it is well established law that a claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. *See Verdegaal Bros. V. Union Oil Co. of California*, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).

The Office Action states that the specification does not contain a precise description of what pH must be included or excluded from the recitation of 'about' pH 5.0. The Office is respectfully directed to the specification at page 8, lines 14-17. As noted therein, "(t)he term 'about'... (i)n the context of numerical values...may be construed to estimate a value that is $\pm 10\%$ of the value or range recited."

Following this definition, Shantz's pH of 4.2 cannot be viewed as being encompassed within the scope of "about pH 5.0" as recited in the instant claims. It is respectfully submitted that the Shantz disclosure does not anticipate the instant claims and it is respectfully requested that this rejection be withdrawn.

Argument regarding room temperature

Applicants do not fully understand the statement in the February 26, 2003, Office Action, Paragraph 6, third paragraph (page 3), that “non-preferable room temperatures do not exclude, for example, 10 degree centigrade, which based on locality, is room temperature.” The only temperature range that Shantz states a preferable room temperature of 18°- 24°C at pH 4.2. Shantz does not state any “non-preferable” room temperature, nor does it disclose 0°-10°C. As noted above, in order for a reference to anticipate, each and every element of the claim must be disclosed.

Paragraph 10 of the Office Action mailed on June 5, 2002, states “that Shantz’s room temperature falls between the claimed range of 10-30 degrees centigrade or even between 0-10 degrees centigrade, based on location, is inherent from the teaching of the prior art.”

MPEP 2131.02 (III) states that (quoting *Continental Can Co. v. Monsanto Co.*, 948 F.2d 1264, 1268 (Fed. Cir. 1991)) “(t)o serve as an anticipation when the reference is silent about the asserted inherent characteristic, such gap in the reference may be filled with recourse to extrinsic evidence. Such evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that is would be so recognized by persons of ordinary skill in the art.” The Office has not provided any extrinsic evidence that the Shantz disclosure inherently discloses the temperature range noted above, other than merely to state “...0-10 degrees centigrade, based on location, is inherent from the teaching of the prior art.”

One skilled in the art would not consider 0°-10°C to fall within the range of room temperature. Hawley’s Condensed Chemical Dictionary, 12th edition, page 1011, defines “room temperature” as “(a)n ambient temperature from 20 to 25 C (68-77F).” A copy of this definition is attached to the end of this paper. 0°-10°C (32°-50°F) is well outside the temperature 20°-25°C as defined by Hawley’s and well outside the 18°-24°C disclosed in

Shantz. There is no evidence that the 0°-10°C range would be recognized by one skilled in the art as necessarily present in the Shantz reference as a “non-preferable” room temperature.

Accordingly, since Shantz does not specifically or inherently disclose the temperature range 0°-10°C, it is respectfully submitted that the Shantz disclosure does not anticipate the instant claims. Withdrawal of this rejection is respectfully requested.

Summary

In summary, the Schantz formulations have problems that have been solved by this invention. First, Schantz teaches a formulation having a pH 4.2 that is stable at room temperature (preferably 18-24°C). Claim 1 is directed to a formulation with a pH between about pH 5 and pH 6 that is stable for at least one year at 0-10 °C. Second, Schantz teaches a formulation having pH 6.2 loses toxicity after a few days at room temperature (18-24°C). Claim 16 is directed to a formulation with a pH between about pH 5 and pH 6 that is stable for at least 6 months at a temperature between about 10-30°C.

Shantz does not anticipate the present claims for the reasons set forth above. Accordingly, it is respectfully submitted that this §102(b) rejection is in error and it is respectfully requested that it be withdrawn against Claims 1-3, 5, 8, 14-17, 21 and 27.

Claim Objections

Claims 4, 6, 7, 9-13, 18-20, 22-26 and 28 are objected to for being dependent on a rejected claim. In light of the above remarks, it is respectfully submitted that this rejection is now moot and Applicants respectfully request that it be withdrawn.

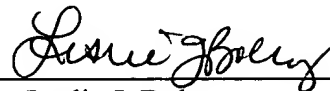
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Conclusion

For the reasons set forth above it is submitted that this case is now in condition for allowance. Early notice to that effect is respectfully requested.

Respectfully submitted,

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Leslie J. Boley
Registration No. 41,490
Tel. no. 650-866-2773

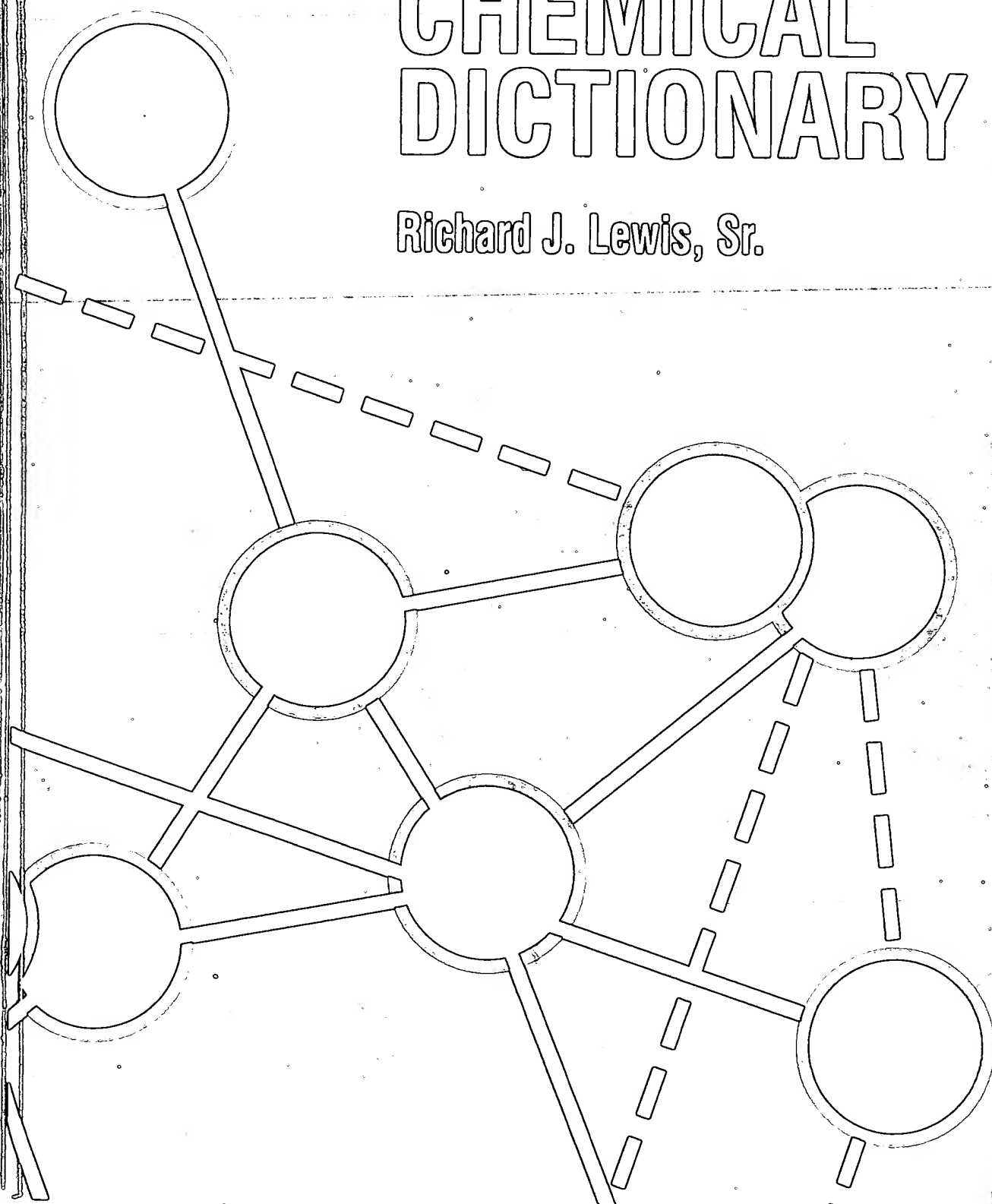
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rocket fuel. (rocket propellant). A substance or mixture that has the capacity for extremely rapid but controlled combustion, which produces large volumes of gas at high pressure and temperature. Rocket fuel is either liquid, solid, or combinations of both. Liquid monopropellants are hydrogen peroxide and hydrazine, catalyzed by finely divided metals to decompose them into gases. Liquid bipropellants consist of the fuel and an oxidizer; typical fuels of this type are hydrogen, hydrazine, ammonia, and boron hydride, the oxidizers being oxygen, nitric acid, ozone, hydrogen peroxide, and water.

Solid propellants include nitrocellulose, plasticized with nitroglycerin or various phthalates; inorganic salts suspended in a plastic or synthetic rubber (e.g., "Thiokol") and containing a finely divided metal. The inorganic oxidizers used are ammonium and potassium nitrates and perchlorates.

Rockwell hardness. See hardness.

rodenticide. A pesticide used to kill rats and other rodents.
See warfarin, squill.

rod mill. A closed steel cylinder one-third filled with rods of about the same length as the cylinder and 1-2 inches in diameter. As the cylinder rotates, the rods roll over one another, exerting a combination of impact and grinding action on the charge. It gives a product of 50-60 mesh with a minimum of fines. Rod mills are used for pulp grinding in the paper industry and for size reduction of ores, minerals, metal powders, etc.

roentgen. (r). The international unit of quantity or dose for both x-rays and γ -rays. It is defined as the quantity of x- or γ -rays which will produce as a result of ionization one electrostatic unit of electricity of either sign in 1 cc (0.001293 g) of dry air as measured at 0°C and standard atmospheric pressure. The use of the roentgen unit has been extended to include particle radiation such as α and β particles and protons and neutrons.
See also rad, curie.

Roentgen, W. K. (1845-1923). A German physicist who discovered x-rays in 1895 for which he was awarded the Nobel prize in 1901. Application of these to a number of important problems in analytical chemistry was developed by the Braggs, Moseley, von Laue, and Debye and Sherrer.

Rohrbach solution.

Properties: Clear, yellow liquid, very refractive, d_{20}^{20} 3.5.

Derivation: An aqueous solution of mercuric barium iodide.

Hazard: Toxic by ingestion and inhalation.

Use: Separating minerals by their specific gravity, microchemical detection of alkaloids.

roll mill. Two chilled steel rolls 48-72 inches wide and 12-24 inches in diameter, turning in opposite directions at different speeds to exert shearing action; the separation (or nip) is adjustable by set screws. As the shearing friction generates considerable heat, the rolls are water-cooled. Such mills are standard equipment in the rubber, plastic, and adhesive industries, several usually rotating on one shaft. They can be used for mixing, but their chief use is for pre-warming calender and extruder feed. Mills with three rolls are used for mixing and grinding paints and printing inks. Laboratory sizes of all types are available.

RON. Abbreviation for research octane number.

ronnell. (O,O-dimethyl-O-(2,4,5-trichlorophenyl)phosphorothioate). CAS: 299-84-3.
 $(\text{CH}_3\text{O})_2\text{P}(\text{S})\text{OC}_6\text{H}_2\text{Cl}_3$.

Properties: Powder or granules, mp 41°C, insoluble in water, soluble in most organic solvents.

Hazard: Toxic by ingestion and inhalation. Cholinesterase inhibitor, use may be restricted.

TLV: 10 mg/m³ of air.

Use: Insecticide.

room temperature. An ambient temperature from 20 to 25°C (68-77°F).

rosaniline. CAS: 632-99-5.

$\text{HOC}(\text{C}_6\text{H}_4\text{NH}_2)_2\text{C}_6\text{H}_3(\text{CH}_3)\text{NH}_2$. A triphenylmethane dye.

Properties: Reddish-brown crystals, mp 186°C (decomposes), soluble in acids and alcohol, slightly soluble in water.

Use: Dye (usually as the hydrochloride), fungicide.

roscoelite. $\text{K}_2\text{V}_4\text{Al}_2\text{Si}_6\text{O}_{20}(\text{OH})_4$. A vanadium-bearing species of mica. Formula variable with V_2O_5 up to 28%. Occurs as minute scales with micaceous cleavage, dark green to brown in color, pearly luster, Mohs hardness 2.5, d_{10}^{20} 3.0.

Occurrence: Colorado, California, Australia.

Use: Source of vanadium.

Rose Bengal. CAS: 11121-48-5.

$\text{C}_{20}\text{H}_4\text{Cl}_4\text{I}_4\text{O}_5$. CI 45440

Properties: Bluish-pink powder, soluble in water.
Use: Biological stain, colorant for inks, cellulose, foods, cosmetics, medicine (diagnostic aid).

Rosenheim color test. On addition of nine parts of trichloroacetic acid in water to a solution of ergosterol in chloroform, an immediate red